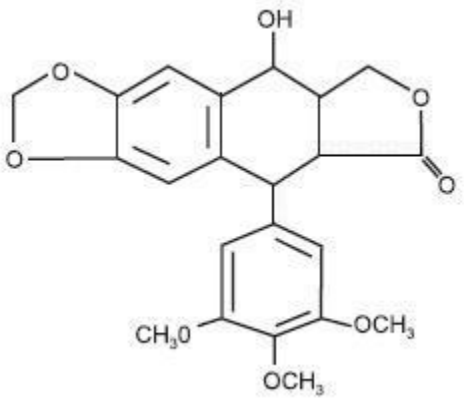
CONDYLOX - podofilox solution
Watson Pharmaceuticals, Inc.

Rx only
128715-1107
Condylox®
(con' de lox)
(podofilox)
0.5% Topical Solution

DESCRIPTION

Condylox is the brand name of podofilox, an antimitotic drug which can be chemically synthesized or purified from the plant families *Coniferae* and *Berberidaceae* (e.g. species of *Juniperus* and *Podophyllum*). Condylox 0.5% Solution is formulated for topical administration. Each milliliter of solution contains 5 mg of podofilox, in a vehicle containing lactic acid and sodium lactate in alcohol 95%, USP.

Podofilox has a molecular weight of 414.4 daltons, and is soluble in alcohol and sparingly soluble in water. Its chemical name is 5,8,8a,9-Tetrahydro-9-hydroxy-5-(3,4,5-trimethoxyphenyl)furo[3',4':6,7] naphtho[2,3,d]-1, 3-dioxol-6(5aH)-one. Podofilox has the following structural formula:



CLINICAL PHARMACOLOGY

Mechanism of Action

Treatment of genital warts with podofilox results in necrosis of visible wart tissue. The exact mechanism of action is unknown.

Pharmacokinetics

In systemic absorption studies in 52 patients, topical application of 0.05 mL of 0.5% podofilox solution to external genitalia did not result in detectable serum levels. Applications of 0.1 to 1.5 mL resulted in peak serum levels of 1 to 17 ng/mL one to two hours after application. The elimination half-life ranged from 1.0 to 4.5 hours. The drug was not found to accumulate after multiple treatments.

CLINICAL STUDIES

In clinical studies with Condylox Solution, the test product and its vehicle were applied in a double-blind fashion to comparable patient groups. Patients were treated for two to four weeks, and reevaluated at a two-week follow-up examination. Although the number of patients and warts evaluated at each time period varied, the results among investigators were relatively consistent.

The following table represents the responses noted in terms of frequency of response by lesions treated and the overall response by patients. Data are presented for the 2-week follow-up only for those patients evaluated at that time point.

Responses in Treated Patients

	Initially Cleared*	Recurred after Clearing*	Cleared at 2-Week Follow-up*
% Warts (n=524)	79% (412/524)	35% (146/412)	60% (269/449)
% Patients (n=70)	50% (35/70)	60% (21/35)	25% (14/57)

*Cleared and clearing mean no visible wart tissue remained at the treated sites

INDICATIONS AND USAGE

Condylox 0.5% Solution is indicated for the topical treatment of external genital warts (Condyloma acuminatum). This product is *not* indicated in the treatment of perianal or mucous membrane warts (see**PRECAUTIONS**).

Diagnosis

Although genital warts have a characteristic appearance, histopathologic confirmation should be obtained if there is any doubt of the diagnosis. Differentiating warts from squamous cell carcinoma (so-called "Bowenoid papulosis") is of particular concern. Squamous cell carcinoma may also be associated with human papillomavirus but should not be treated with Condylox 0.5% Solution.

CONTRAINDICATIONS

Condylox 0.5% Solution is contraindicated for patients who develop hypersensitivity or intolerance to any component of the formulation.

WARNINGS

Correct diagnosis of the lesions to be treated is essential. See the "**Diagnosis**" subsection of the**INDICATIONS AND USAGE** statement.

Condylox 0.5% Solution is intended for cutaneous use only. **Avoid contact with the eye. If eye contact occurs, patients should immediately flush the eye with copious quantities of water and seek medical advice.**

PRECAUTIONS

General

Data are not available on the safe and effective use of this product for treatment of warts occurring in the perianal area or on mucous membranes of the genital area (including the urethra, rectum and vagina). The recommended method of application, frequency of application, and duration of usage should not be exceeded (see**DOSAGE AND ADMINISTRATION**).

Information for Patients

The patient should be provided with a Patient Information leaflet when a Condylox prescription is filled.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Reports of lifetime carcinogenicity studies in mice are not available. Published animal studies, in general, have not shown the drug substance, podofilox, to be carcinogenic.[1,2,3,4,5] There are published reports that, in mouse studies, crude podophyllin resin (containing podofilox) applied topically to the cervix produced changes resembling carcinoma *in situ*.[6] These changes were reversible at five weeks after cessation of treatment. In one reported experiment, epidermal carcinoma of the vagina and cervix was found in 1 out of 18 mice after 120 applications of podophyllin[7] (the drug was applied twice weekly over a 15-month period).

Podofilox was not mutagenic in the Ames plate reverse mutation assay at concentrations up to 5 mg/plate, with and without metabolic activation. No cell transformation related to potential oncogenicity was observed in BALB/3T3 cells after exposure to podofilox at concentrations up to 0.008 μg/mL without metabolic activation and 12 μg/mL podofilox with metabolic activation. Results from the mouse micronucleus *in vivo* assay using podofilox 0.5% solution in concentrations up to 25 mg/kg, indicate that podofilox should be considered a potential clastogen (a chemical that induces disruption and breakage of chromosomes).

Daily topical application of Condylox 0.5% Solution at doses up to the equivalent of 0.2 mg/kg (5 times the recommended maximum human dose) to rats throughout gametogenesis, mating, gestation, parturition and lactation for two generations demonstrated no impairment of fertility.

Pregnancy

Category C: Podofilox was not teratogenic in the rabbit following topical application of up to 0.21 mg/kg (5 times the maximum human dose) once daily for 13 days. The scientific literature contains references that podofilox is embryotoxic in rats when administered systemically in a dose approximately 250 times the recommended maximum human dose.[8,9] Teratogenicity and embryotoxicity have not been studied with intravaginal application. Many antimitotic drug products are known to be embryotoxic. There are no adequate and well-controlled studies in pregnant women. Podofilox should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from podofilox, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

In clinical trials, the following local adverse reactions were reported at some point during treatment.

Adverse Experience	Males	Females
Burning	64%	78%
Pain	50%	72%
Inflammation	71%	63%
Erosion	67%	67%
Itching	50%	65%

Reports of burning and pain were more frequent and of greater severity in women than in men.
Adverse effects reported in less than 5% of the patients included pain with intercourse, insomnia, tingling, bleeding, tenderness, chafing, malodor, dizziness, scarring, vesicle formation, crusting edema, dryness/peeling, foreskin irretraction, hematuria, vomiting and ulceration.

OVERDOSAGE

Topically applied podofilox may be absorbed systemically (see**CLINICAL PHARMACOLOGY** section). Toxicity reported following systemic administration of podofilox in investigational use for cancer treatment included: nausea, vomiting, fever, diarrhea, bone marrow depression, and oral ulcers. Following 5 to 10 daily intravenous doses of 0.5 to 1 mg/kg/day, significant hematological toxicity occurred but was reversible. Other toxicities occurred at lower doses. Toxicity reported following systemic administration of podophyllum resin included: nausea, vomiting, fever, diarrhea, peripheral neuropathy, altered mental status, lethargy, coma, tachypnea, respiratory failure, leukocytosis, pancytosis, hematuria, renal failure, and seizures. Treatment of topical overdosage should include washing the skin free of any remaining drug and symptomatic and supportive therapy.

DOSAGE AND ADMINISTRATION

In order to ensure that the patient is fully aware of the correct method of therapy and to identify which specific warts should be treated, the technique for initial application of the medication should be demonstrated by the prescriber.
Apply twice daily morning and evening (every 12 hours), for 3 consecutive days, then withhold use for 4 consecutive days. This one week cycle of treatment may be repeated up to four times until there is no visible wart tissue**. If there is incomplete response after four treatment weeks, alternative treatment should be considered. Safety and effectiveness of more than four treatment weeks have not been established.**
Condylox 0.5% Solution is applied to the warts with a cotton-tipped applicator supplied with the drug. The drug-dampened applicator should be touched to the wart to be treated, applying the minimum amount of solution necessary to cover the lesion. **Treatment should be limited to less than 10 cm^2 of wart tissue and to no more than 0.5 mL of the solution per day.** There is no evidence to suggest that more frequent application will increase efficacy, but additional applications would be expected to increase the rate of local adverse reactions and systemic absorption.
Care should be taken to allow the solution to dry before allowing the return of opposing skin surfaces to their normal positions. After each treatment, the used applicator should be carefully disposed of and the patient should wash his or her hands.

HOW SUPPLIED

3.5 mL of Condylox 0.5% Solution is supplied as a clear liquid in amber glass bottles with child-resistant screw caps. NDC 52544-046-13. Store at controlled room temperature between 15 - 30°C (59 - 86°F). **Avoid excessive heat. Do not freeze.**
Rx only

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